Challenges of prioritising reference materials

Standardisation of Genome Amplification Technologies Meeting
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Production of Reference Materials

Prioritize

- **Selection of reference material**
- Produce/obtain candidate material(s)
- Appropriate/relevant matrix
- Characterization properties & methods
- Homogeneous
- Stable
- Commutable

Efficient and targeted prioritization is key

Timeframe (NIST) at least 18-36 months if all goes well

Feedback is important

- **Interactions at professional meetings & societies**
- Survey
- Industry
- International community (WHO)
- Direct request/contacts

Knowledge/cataloging of what materials are currently available & what is under development

List of priorities from AMP

Clinical Practice Committee, AMP June 2009

- Example 1: Targeted therapeutics and tumor markers
  - *BCR-ABL, JAK2*
- Example 2: Companion Dx
  - *KRAS, EGFR*
- Example 3: Transplant follow-up care and quantitative standards
  - CMV, EBV, BKV
- Example 4: Reference gene sequence database
  - Alternative to GenBank; better associate with clinical labs

AMP Association for Molecular Pathology

http://www.amp.org/

List of priorities from AMP (2009)

- Immediate
  - CMV, *BCR/ABL, KRAS, EGFR*
- Medium term (One year)
  - BKV, EBV
- Long term (1-3 years)
  - Adenovirus, Enterovirus, Hep B, HSV 1&2, HHV-6/7/8, HTLV 1&2, HMPV, JCV, Influenza virus, Parvovirus B19, RSV, VZV

Feedback is important

- Interactions at professional meetings & societies
- **Survey**
- Industry
- International community
- Direct request/contacts

- 14 Questions
- 70 responses
- ‘Market research’ on virology field and reference materials (what is needed, strains, etc)
- **Distribution**

- Association for Molecular Pathology (AMP)
- Pan-Atlantic Society for Clinical Virology (PASCV)
- European Molecular Genetics Quality Network (EMQN)
- Eurogentest
- UK Genetics Lab Directors
- American Society of Human Genetics (ASHG)

Selected questions

1) Which company or testing laboratory do you represent?

2) What best describes your affiliation?

3) What is your perception of the purpose of a primary reference material?

(**77% - yes**)

4) Do you use *primary reference materials* in your work?

5) If so, from where do you purchase your reference materials?

6) For what purposes do you use primary reference materials?

Selected questions

7) For which viruses, microbes, cancers, genetic diseases, or other disease/organism does your laboratory or company currently use reference materials?

8) Do you think that primary reference materials are a necessity in the clinical community? (**93% - yes**)

9) What is your preferred matrix (specimen type) for a reference material?

10) If a reference material in your preferred matrix is unavailable, would extracted DNA/RNA in a buffer work for your purposes? (**71% - yes**)

Selected questions

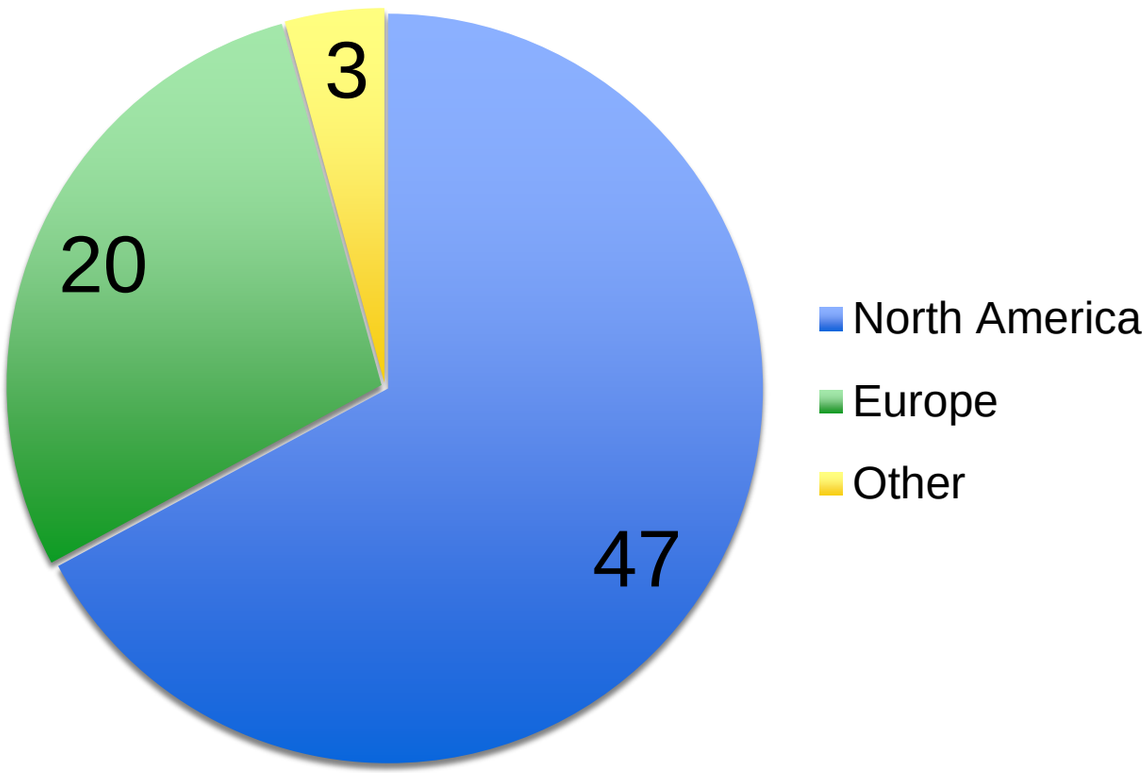
11) If you work with viruses, would you rather have **multiple materials** of different genotypes of a virus or **one material** with a conserved region of the viral genome? 12) If yes, please explain

13) What other primary reference materials do you think the clinical community lacks?

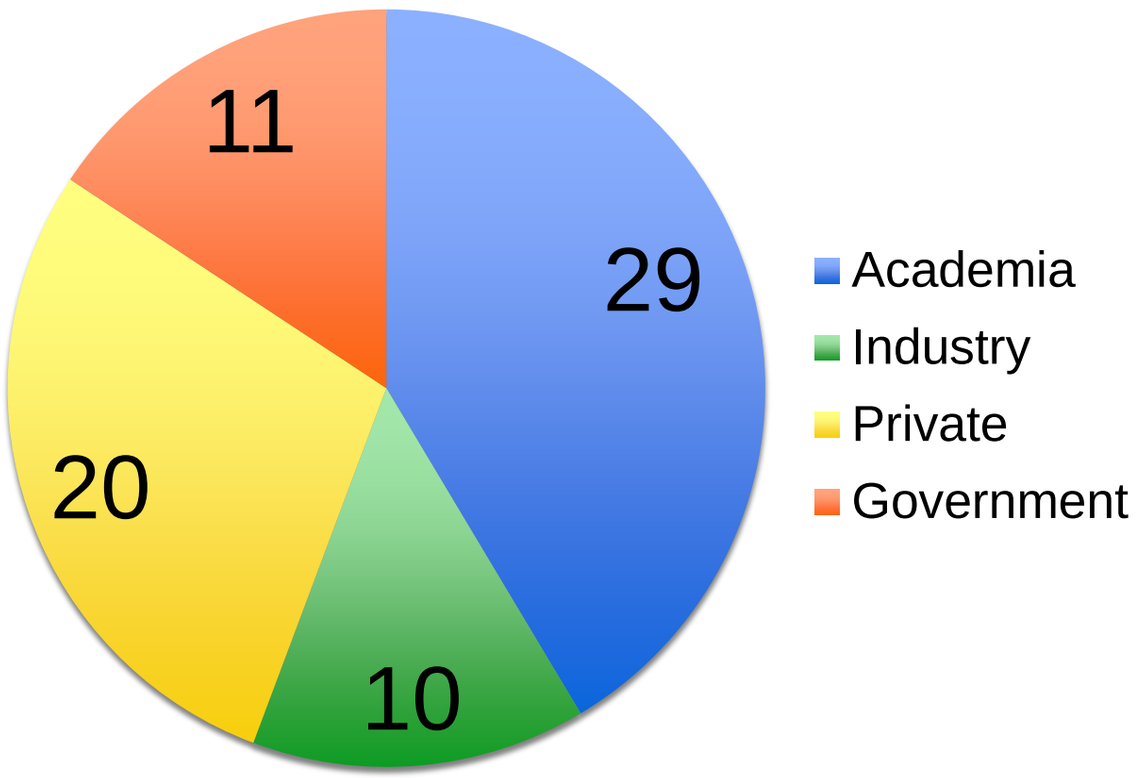
14) Other comments or suggestions.

General Information

Location of respondent



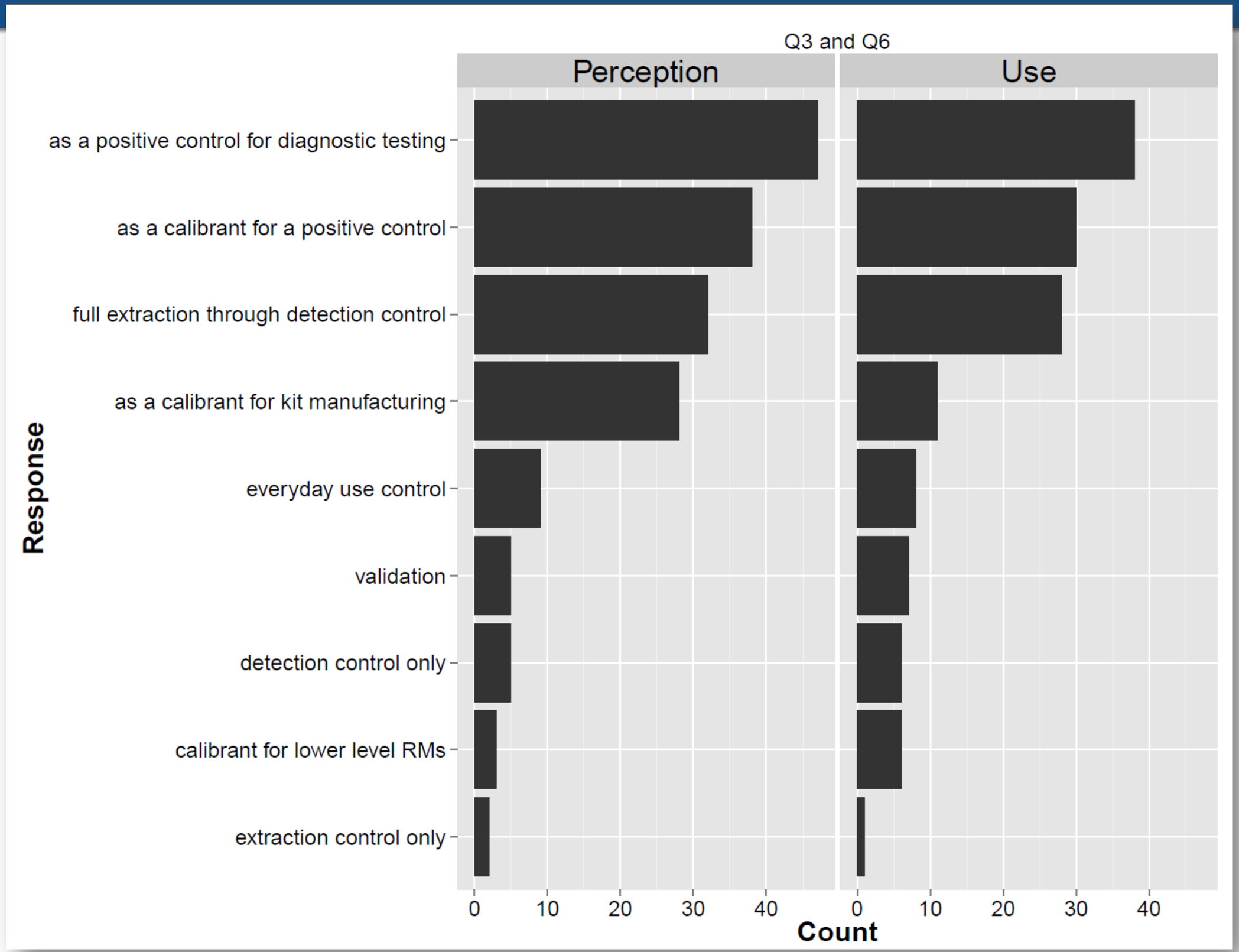
What best describes your affiliation?



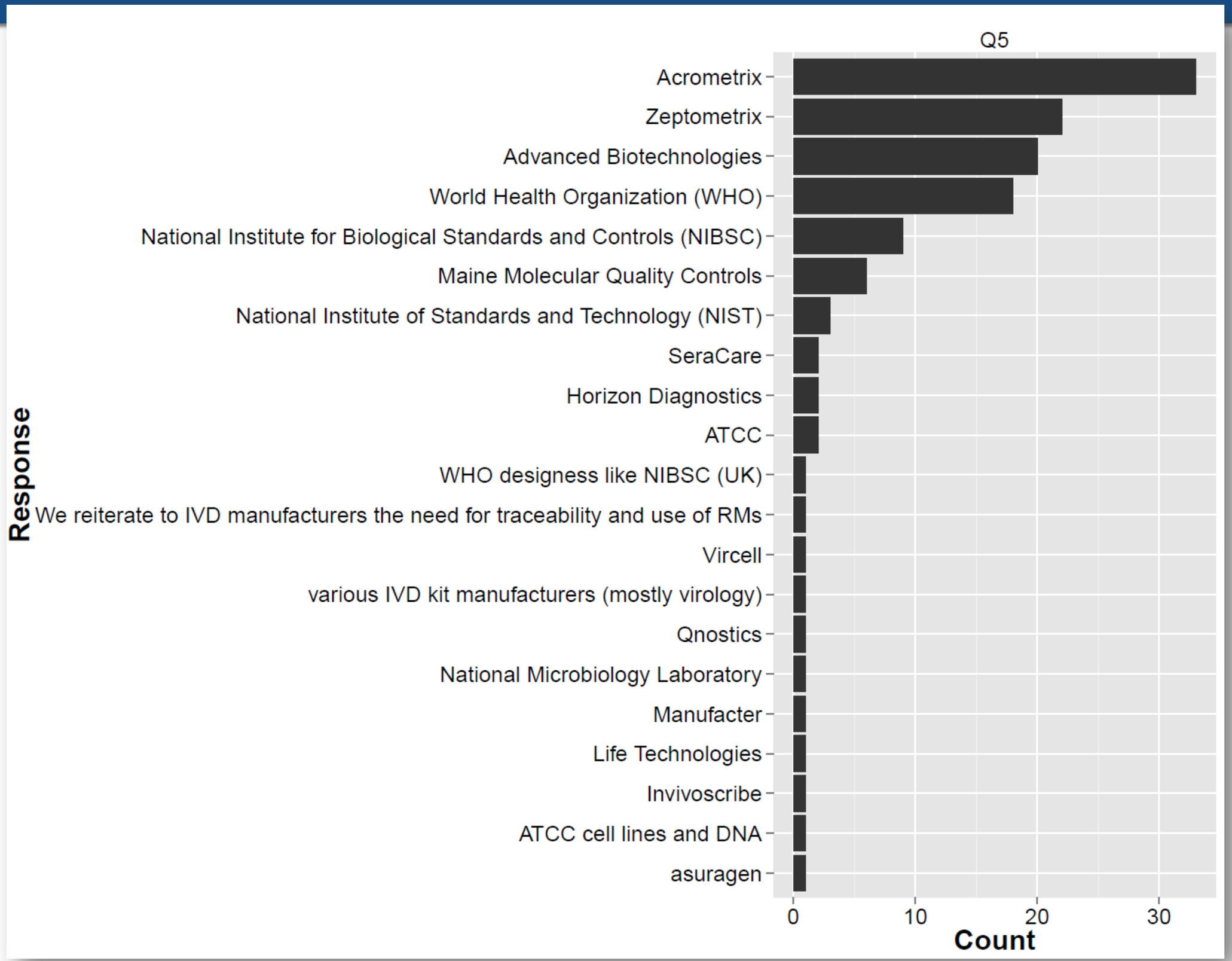
n=70

Your perception of the purpose of a primary reference material?
For what purposes do you use primary reference materials?

Multiple selections were possible

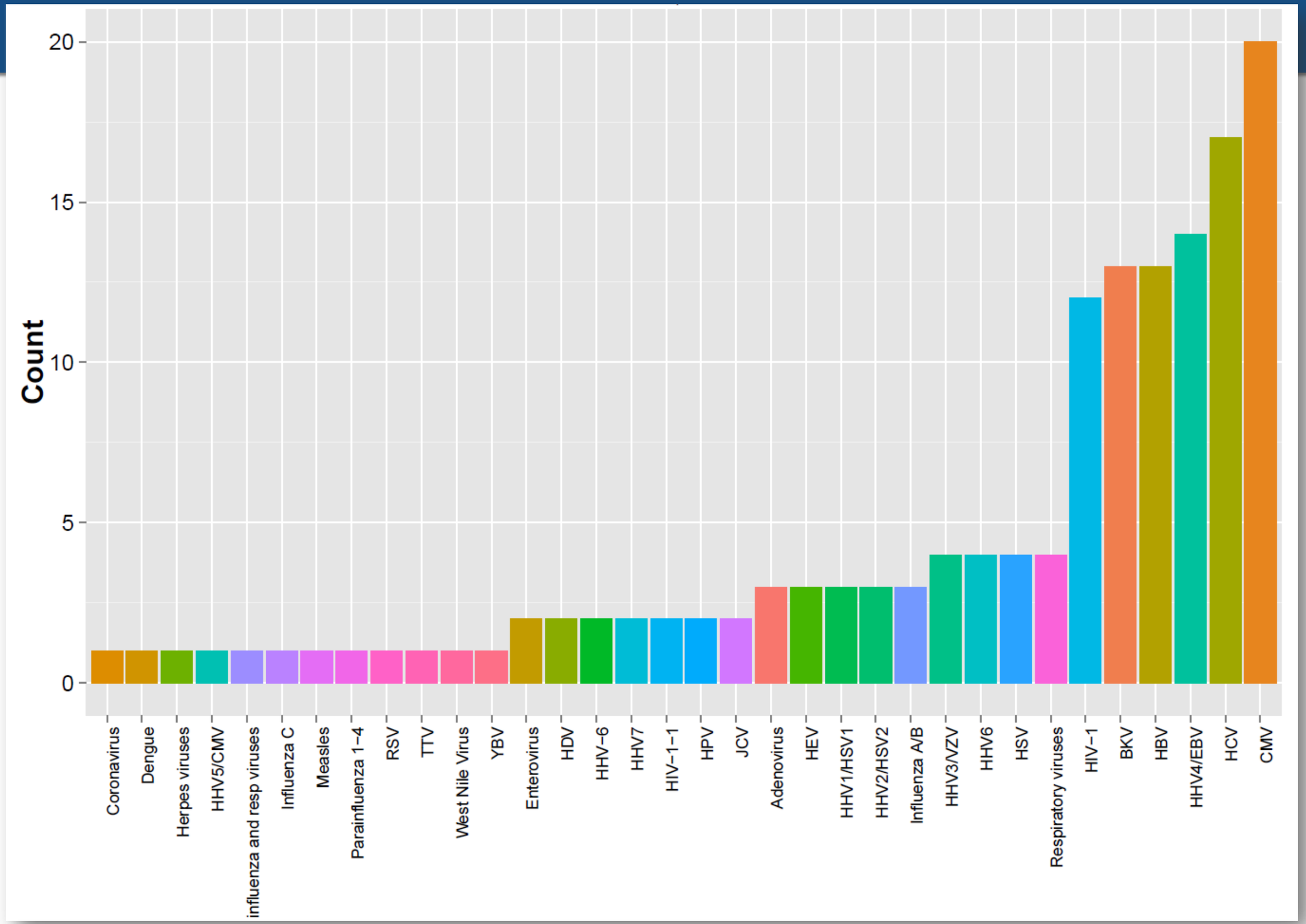


Where do you purchase your reference materials?



Multiple materials of different genotypes of a virus or one material with a conserved region of the viral genome?

For which viruses does your laboratory or company currently use reference materials?



What other primary reference materials do you think the community lacks?

- HHV6, BKV (2), HSV, VZV
- Dengue
- “I find it hard to answer this question”
- “I found all what I need today”

- Cancer mutation panels
- “Good Bcr-Abl”
- microRNA
- Fragile X
- Reference Genome
- Cystic fibrosis

Sampling of Comments

- “There ought to be concerted international effort to standardise quantitative testing like how it has been achieved for HIV, HBV, HCV, EBV and CMV.”

- “I think not only is there a need for more Primary RMs but there should be good guidance on the use of these so that they are used appropriately. In the clinical lab setting, I see their use ideally being for the preparation of lower level RMs.”

- “Prefer product be available through common vendors, e.g. ThermoFisherScientific etc.”

Sampling of Comments

- “There is a lack of information on what targets institutes are working, so the timeframe info is important. A lot of labs are currently taking a lot of initiatives and spending a lot of money. Another issue is the info on commutability of the reference material.”

- “The cost of purchasing appropriate controls would be a factor in moving forward.”

- “I wonder if it is possible to truly capture the complexities and heterogeneity present in most disease states with a single reference.”

SoGAT Fall 2009

For the majority of clinical NAT-based assays no higher order reference standards exist. The SoGAT Clinical Diagnostics Working Group has been established to help coordinate the development of reference materials to standardise NAT-based assays for clinically-relevant pathogens. Progress is already being made to develop the 1st WHO International Standards for human cytomegalovirus and Epstein-Barr virus. While there is a need to develop standards for a number of clinical targets we would like to prioritise their development in consideration of the global clinical need and health impact.

We would like you to **name one pathogen** for which you feel there is a need to standardise current molecular assays through the development of an International Standard, and state the **reason for this selection** (reply by email to SoGAT@nibsc.hpa.org.uk by 31st August 2009, including the type of laboratory which you represent). The results from this survey will form part of a discussion on prioritising the development of reference materials for NAT assays for clinical pathogens, at the forthcoming SoGAT Clinical Diagnostics meeting in Istanbul on 30th September and 1st October 2009 (www.nibsc.ac.uk/partners/SoGAT).

Thank you in advance,

SoGAT Clinical Diagnostics Organising Committee

Summarized Results from SoGAT survey (2009)

- C. trachomatis and/or N. gonorrhoeae
- West Nile Virus (2)
- Toxoplasma gondii
- Hepatitis D Virus
- Adenovirus
- BK Virus (3)
- Influenza A Virus
- Human Herpesvirus 8
- Norovirus
- Hepatitis E Virus (2)
- JC Virus

Discussion

- Surveys can provide insightful data, but can also be **biased** based on questions, context, level of participation, narrow audience, etc.

- Perception of **primary reference materials**

  - **Need to clearly define 1° versus 2° reference materials**

- How do we best prioritize future primary reference materials?

  - What is currently available and in process

  - Take in all feedback

  - Weight: impact, immediacy, time, cost; what requires a 1° material?

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